

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

| | |
|--|--|
| Date of mailing (day/month/year) 31 May 2001 (31.05.01) | |
| International application No. PCT/US00/40165 | Applicant's or agent's file reference |
| International filing date (day/month/year) 08 June 2000 (08.06.00) | Priority date (day/month/year) 08 June 1999 (08.06.99) |
| Applicant WHITLEY, Richard, J. et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

02 January 2001 (02.01.01)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

| | |
|---|---|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 | Authorized officer Olivia TEFY Telephone No.: (41-22) 338.83.38 |
|---|---|

PATENT COOPERATION TREATY

PCT

REC 16 OCT 2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | | |
|--|---|---|--|
| Applicant's or agent's file reference UAB-16152/22 | | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/US00/40165 | International filing date (day/month/year) 08 June 2000 (08.06.2000) | Priority date (day/month/year) 08 June 1999 (08.06.1999) | |
| International Patent Classification (IPC) or national classification and IPC IPC(7): C 12 N 7/00, 15/00; C 12 Q 1/68; C 07 K 1/00. and US Cl.: 435/320.1, 6, 69.1; 514/44; 424/93.2, 93.21. | | | |
| Applicant UAB RESEARCH FOUNDATION | | | |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p> | | | |
| <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p> | | | |
| Date of submission of the demand 02 January 2001 | | Date of completion of this report 17 September 2001 | |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230 | | Authorized officer Eleanor Sorbello Telephone No. 703-308-0196 SCOTT D. PRIEPE, PH.D PRIMARY EXAMINER Scott D. Prieppe for | |

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/40165

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-24 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages 25-27, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the drawings:
pages 1-7, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/40165

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

| | | |
|-------------------------------|--------------------|-----|
| Novelty (N) | Claims <u>NONE</u> | YES |
| | Claims <u>1-15</u> | NO |
| Inventive Step (IS) | Claims <u>NONE</u> | YES |
| | Claims <u>1-15</u> | NO |
| Industrial Applicability (IA) | Claims <u>1-15</u> | YES |
| | Claims <u>NONE</u> | NO |

2. CITATIONS AND EXPLANATIONS (Rule 70.7)

Claims 1-15 lack novelty under PCT Article 33(2) as being anticipated by Toda et al. Toda et al. teach intratumoral administration of a replication competent HSV encoding IL-12 wherein the HSV comprises a deletion in the γ_1 34.5 gene. Toda et al. also teach antitumoral activity wherein the cancer vaccine comprising the HSV comprising a deletion in the γ_1 34.5 gene further comprising a heterodimeric cytokine IL-12, comprising 35 kDa (p35) and 40kDa (p40) subunits.

----- NEW CITATIONS -----

PATENT COOPERATION TREATY

RECEIVED
 OCT 15 2001
 GIFFORD, KRASS, GROH, SPRINKLE,
 ANDERSON & CITKOWSKI, P.C.

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
ELLEN S. COGEN
GIFFORD, KRASS, GROH, SPRINKLE, ANDERSON
CITKOWSKI, P.C.
280 N OLD WOODWARD AVE., STE. 400
BIRMINGHAM, MI 48009

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

| | |
|-------------------------------------|-------------|
| Date of Mailing (day/month/year) | 12 OCT 2001 |
|-------------------------------------|-------------|

Applicant's or agent's file reference

UAB-16152/22

IMPORTANT NOTIFICATION

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US00/40165

08 June 2000 (08.06.2000)

08 June 1999 (08.06.1999)

Applicant

UAB RESEARCH FOUNDATION

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

SCOTT D. PRIEBE, PH.D

~~PRIMARY EXAMINER~~

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Eleanor Sorbello

Telephone No. 703-308-0196

Scott D. Priebe for

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | |
|---|---|--|
| Applicant's or agent's file reference UAB-16152/22 | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/US00/40165 | International filing date (day/month/year) 08 June 2000 (08.06.2000) | Priority date (day/month/year) 08 June 1999 (08.06.1999) |
| International Patent Classification (IPC) or national classification and IPC IPC(7): C 12 N 7/00, 15/00; C 12 Q 1/68; C 07 K 1/00. and US Cl.: 435/320.1, 6, 69.1; 514/44; 424/93.2, 93.21. | | |
| Applicant UAB RESEARCH FOUNDATION | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the report
 - II ☐ Priority
 - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

| | |
|---|---|
| Date of submission of the demand 02 January 2001 | Date of completion of this report 17 September 2001 |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230 | Authorized officer Eleanor Sorbello Telephone No. 703-308-0196 SCOTT D. PRIEBE, PH.D. PRIMARY EXAMINER <i>Scott D. Pribe for</i> |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/40165

I. Basis of the report

1. With regard to the elements of the international application: *

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-24 _____ as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☒ the claims:
pages 25-27 _____, as originally filed
pages NONE _____, as amended (together with any statement) under Article 19
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☒ the drawings:
pages 1-7 _____, as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE _____, as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)). **

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/40165

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

| | | |
|-------------------------------|--------------------|-----|
| Novelty (N) | Claims <u>NONE</u> | YES |
| | Claims <u>1-15</u> | NO |
| Inventive Step (IS) | Claims <u>NONE</u> | YES |
| | Claims <u>1-15</u> | NO |
| Industrial Applicability (IA) | Claims <u>1-15</u> | YES |
| | Claims <u>NONE</u> | NO |

2. CITATIONS AND EXPLANATIONS (Rule 70.7)

Claims 1-15 lack novelty under PCT Article 33(2) as being anticipated by Toda et al. Toda et al. teach intratumoral administration of a replication competent HSV encoding IL-12 wherein the HSV comprises a deletion in the γ_1 34.5 gene. Toda et al. also teach antitumoral activity wherein the cancer vaccine comprising the HSV comprising a deletion in the γ_1 34.5 gene further comprising a heterodimeric cytokine IL-12, comprising 35 kDa (p35) and 40kDa (p40) subunits.

----- NEW CITATIONS -----

ATENT COOPERATION TREA

RECEIVED
SEP 04 2001

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
ELLEN S. COGEN
GIFFORD, KRASS, GROH, SPRINKLE, ANDERSON
CITKOWSKI, P.C.
280 N OLD WOODWARD AVE., STE. 400
BIRMINGHAM, MI 48009

PCT GIFFORD, KRASS, GROH, SPRINKLE,
ANDERSON & CITKOWSKI, P.C.

WRITTEN OPINION

(PCT Rule 66)

| | | |
|---|---|--|
| Applicant's or agent's file reference UAB-16152/22 | | Date of Mailing (day/month/year) 29 AUG 2001 REPLY DUE within .L. months/days from: the above date of mailing |
| International application No. PCT/US00/40165 | International filing date (day/month/year) 08 June 2000 (08.06.2000) | Priority date (day/month/year) 08 June 1999 (08.06.1999) |
| International Patent Classification (IPC) or both national classification and IPC IPC(7): C 12 N 7/00, 15/00; C 12 Q 1/68; C 07 K 1/00. and US Cl.: 435/320.1, 6, 69.1; 514/44; 424/93.2, 93.21. | | |
| Applicant UAB RESEARCH FOUNDATION | | |

Response to Written Opn due 9-29-01

- This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.
- This opinion contains indications relating to the following items:
 - ☒ Basis of the opinion
 - ☐ Priority
 - ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Lack of unity of invention
 - ☒ Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Certain documents cited
 - ☐ Certain defects in the international application
 - ☐ Certain observations on the international application
- The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
- The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 08 October 2001 (08.10.2001).

| | |
|---|--|
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230 | Authorized officer Eleanor Sorbello Telephone No. 703-308-0196 |
|---|--|

WRITTEN OPINION

International application No.

PCT/US00/40165

I. Basis of the opinion

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☒ the description:
 pages 1-24, as originally filed
 pages NONE, filed with the demand
 pages NONE, filed with the letter of _____.
- ☒ the claims:
 pages 25-27, as originally filed
 pages NONE, as amended (together with any statement) under Article 19
 pages NONE, filed with the demand
 pages NONE, filed with the letter of _____.
- ☒ the drawings:
 pages 1-7, as originally filed
 pages NONE, filed with the demand
 pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
 pages NONE, as originally filed
 pages NONE, filed with the demand
 pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."

WRITTEN OPINION

International application No.
PCT/US00/40165

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

| | | |
|-------------------------------|--------------------|-----|
| Novelty (N) | Claims <u>NONE</u> | YES |
| | Claims <u>1-15</u> | NO |
| Inventive Step (IS) | Claims <u>NONE</u> | YES |
| | Claims <u>1-15</u> | NO |
| Industrial Applicability (IA) | Claims <u>1-15</u> | YES |
| | Claims <u>NONE</u> | NO |

2. CITATIONS AND EXPLANATIONS

Claims 1-15 lack novelty under PCT Article 33(2) as being anticipated by Toda et al. Toda et al. teach intratumoral administration of a replication competent HSV encoding IL-12 wherein the HSV comprises a deletion in the γ_1 34.5 gene. Toda et al. also teach antitumoral activity wherein the cancer vaccine comprising the HSV comprising a deletion in the γ_1 34.5 gene further comprising a heterodimeric cytokine IL-12, comprising 35 kDa (p35) and 40kDa (p40) subunits.

----- NEW CITATIONS -----

WRITTEN OPINION

Intern. application No.
PCT/US00/40165

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Certain Documents Cited

1. Certain published documents (Rule 70.10)

| Application No | Publication Date | Filing Date | Priority date (valid claim) |
|-------------------|-------------------------|-------------------------|-----------------------------|
| <u>Patent No.</u> | <u>(day/month/year)</u> | <u>(day/month/year)</u> | <u>(day/month/year)</u> |
| None | None | None | None |

2. Non-written disclosures (Rule 70.9)

| Kind of non-written disclosure | Date of non-written disclosure | Date of written disclosure referring to non-written disclosure |
|--------------------------------|--------------------------------|--|
| <u>(day/month/year)</u> | <u>(day/month/year)</u> | <u>(day/month/year)</u> |
| None | None | None |

WRITTEN OPINION

Inter. application No.
PCT/US00/40165

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.